

## ***Remarks***

### ***I. Status of the Claims and the Specification***

Upon entry of the foregoing amendments claims 1-15, 19, 21-34, 55 and 61-63 and 68-96 are pending in the application, with claims 1 and 63 being the independent claims. Claims 16-18, 20, 35-54, 56-60 and 64-67 are sought to be cancelled without prejudice to or disclaimer of the subject matter therein. Pending claims 5, 9, 10, 12 and 30 have been withdrawn from consideration by the Examiner as not being directed to an elected species.

Amendment is sought to claims 1, 25, 30, 55, 63, 70-71, and 77, and new claims 91-96 are sought to be entered. These amendments and new claims are supported, *inter alia*, by the originally filed claims and specification. In particular for the currently amended claim 1, the added feature "wherein said ghrelin peptide comprises an amino acid sequence of SEQ ID NO:119" was originally disclosed, *inter alia*, in original claim 25 as filed. For the currently amended claim 63, the added feature "wherein said core particle comprises a virus-like particle of an RNA-bacteriophage" can be found in original claim 2 of the application as filed. Hence these amendments do not introduce new matter, and their entry and consideration are respectfully requested.

### ***II. Summary of the Office Action***

In the Office Action of July 20, 2006 (hereinafter "the Office Action"), at page 2, the Examiner has acknowledged the restriction requirement with the additional species election of SEQ ID NO:4 (a bacteriophage sequence) and SEQ ID NO 65 (ghrelin sequence). It is noted that the Examiner has not fully addressed the traversal of the species election set out in the Response of May 4, 2006. It is Applicants' understanding that the examined species are Q 1700.0340001/BJD/U-W

beta phage, SEQ ID NO:4, SEQ ID NO:31 and SEQ ID NO: 65. Clarification for the record is respectfully requested.

Applicants note that the Examiner has withdrawn claims 61 and 62 as allegedly being drawn to a non-elected invention, specifically, methods of using the composition of Group I set out in the Election/Restriction requirement made in the January 12, 2006 Office Action. In light of the decisions in *In re Ochiai*, 71 F.3d 1565, 37 USPQ2d 1127 (Fed. Cir. 1995) and *In re Brouwer*, 77 F.3d 422, 37 USPQ 2d 1663 (Fed. Cir. 1996), a notice was published in the Official Gazette which set forth the guidelines for the treatment of product and process claims. *See* 1184 OG 86 (March 26, 1996). Specifically, the notice states that in the case of an elected product claim, rejoinder will be permitted when a product claim is found allowable and the withdrawn process claim depends from or otherwise includes all the limitations of an allowed product claim.

Accordingly, Applicants respectfully request that if any of the claims of Group I, *i.e.*, any of pending composition claims 1-4, 6-8, 11, 13-15, 19, 21-29, 31-34, 55, 63-95, are found allowable, that the process claims of claims 61, 62 and newly added claim 96 be rejoined and examined for patentability.

At pages 3-5 of the Office Action the Examiner has withdrawn the rejections made in the previous Office Action under 35 U.S.C. § 101, 112, 102, and 103.

At pages 5-6 of the Office Action the Examiner has objected to claims 63, 64, 66, 68, 69, 70, 71, 72, 76, 77, 78, 79, 80, 81, 82, 83, 84 and 85 as allegedly being substantially duplicative of claims 2, 4, 6, 7, 8, 9-11, 12, 15, 19, 22, 23, 25, 27, 28, 29, 30 and 31 respectively.

At pages 6-10 of the Office Action the Examiner has rejected claims 1-3, 15, 19, 21-31, 32-34, 55, 63, 64, and 76-85 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Sebbel *et al.* (US Patent 6964769, herein "Sebbel") in view of Kojima (Nature, 1999, herein "Kojima"). Furthermore, at pages 10-11 the Examiner has rejected claims 4, 6-8, 11-14, 31, 66, 68-70, 72, 73, 75, and 85 as allegedly being unpatentable under 35 U.S.C. 103(a) over Sebbel *et al.* in view of Kojima *et al.* and further in view of Vasiljeva *et al.* (FEBS Letters, 1998) and Maita *et al.* (Gen Pept Accession VCBPQB, 1971).

In view of the following remarks, Applicants respectfully traverse the Examiner's objections and rejections and respectfully request that they be reconsidered and withdrawn.

### ***III. Claim Objections***

In the Office Action at page 5 the Examiner has objected to claim 63 (Applicants assume that the Examiner has erroneously written claim 61) as being substantially duplicate of claim 1. Applicants respectfully disagree.

As noted in the MPEP, Applicants may restate their invention in a reasonable number of different ways:

Inasmuch as a patent is supposed to be limited to only one invention or, at most, several closely related indivisible inventions, limiting an application to a single claim, or a single claim to each of the related inventions might appear to be logical as well as convenient. However, court decisions have confirmed applicant's right to restate (i.e., by plural claiming) the invention in a reasonable number of ways. Indeed, a mere difference in scope between claims has been held to be enough.

MPEP § 706.03(k) (Rev. 3, Aug. 2005). In the present case, the objection to independent claims 1 and 63 as being substantially duplicative cannot stand, because these two claims differ in scope.

Claim 63 as originally presented recited that the first and second attachment sites in the components of the claimed composition were associated "through at least one non-peptide bond," an element not recited in claim 1 as originally presented. Hence, these two claims as originally presented were of different scope, and the objection to these claims as being "substantial duplicates" is improper under MPEP § 706.03(k).

In any event, for reasons unrelated to this objection, claims 1 and 63 have now been amended in a way that renders this objection moot. Specifically, claim 1 as currently presented recites a specific ghrelin peptide (*i.e.*, SEQ ID NO:119) that is not recited in claim 63 as currently presented; and claim 63 as currently presented recites a core particle that comprises a VLP of an RNA bacteriophage, an element that is not recited in claim 1 as currently presented (in addition to the "non-peptide bond" element recited in claim 63 that is not recited in claim 1). Accordingly, claims 1 and 63 are substantially different in scope, thus rendering moot the objection as it may have been applied to those claims.

The Examiner further objected claims 64, 66, 68, 69, 70, 71, 72, 76, 77, 78, 79, 80, 81, 82, 83, 84 and 85 as being substantially duplicate of claims 2, 4, 6, 7, 8, 9-11, 12, 15, 19, 22, 23, 25, 27, 28, 29, 30 and 31 respectively. Applicants respectfully disagree. As an initial matter, claims 64, 66 and 68 have been cancelled, rendering moot the rejection as it may have been applied to those claims. Applicants traverse the rejection as it may have been applied to the presently pending claims. Since the former group of claims are all dependent claims of claim 63 and the latter group of claims are all dependent claims of claim 1, the former group of claims differ substantially from the latter group of claims. Specifically, for at least the reasons discussed above, claims 1 and 63 are substantially different in scope; hence, the claims that depend from these independent claims are also different in scope. Accordingly,

the objection is improper under MPEP § 706.03(k); it is therefore respectfully requested that the Examiner reconsider and withdraw the objection.

***IV. Rejections under 35 U.S.C. § 103***

***(a) Claims 1-3, 15, 19, 21-31, 32-34, 55, 63, 64, and 76-85 are not rendered obvious under 35 U.S.C. 103(a) by Sebbel et al. in view of Kojima et al.***

In the Office Action at pages 6-10 the Examiner rejected claims 1-3, 15, 19, 21-31, 32-34, 55, 63, 64, and 76-85 under 35 U.S.C. 103(a) as being unpatentable over Sebbel et al., (US Patent 6,964,769 B2, herein, “Sebbel”) in view of Kojima et al. (Nature, 1999, herein, “Kojima”). Applicants respectively disagree. As an initial matter claim 64 has been cancelled, rendering moot the rejection as it may have been applied to this claim. Applicants respectfully traverse the rejection as it may have been applied to the presently pending claims.

The Examiner bears the burden of establishing a *prima facie* case of obviousness based upon the prior art. *See In re Piasecki*, 223 USPQ 785, 787-88 (Fed. Cir. 1984). The Examiner can satisfy this burden only by showing some objective teaching in the prior art, or that knowledge generally available to one of ordinary skill in the art, would lead that individual to combine the relevant teachings of the references in such a way as to produce the invention as claimed. *See In re Fine*, 5 USPQ2d 1596,1598 (Fed. Cir. 1988).

If a combination of references is used to attempt to establish obviousness, there must be “a reason, suggestion, or motivation in the prior art that would lead one of ordinary skill in the art to combine the references, and that would also suggest a reasonable likelihood of success.” *See Smiths Indus. Med. Sys. v. Vital Signs, Inc.*, 183 F.3d 1347, 1356 (Fed. Cir. 1999). “Such a suggestion or motivation may come from the references themselves, from

knowledge by those skilled in the art that certain references are of special interest in a field, or even from the nature of the problem to be solved.” *Id.* at 1347. Although the references “need not expressly teach that the disclosure contained therein should be combined, the showing of combinability must be ‘clear and particular.’” *Ruiz v. A.B. Chance*, 234 F.3d 654, 665 (Fed. Cir. 2000). A rigorous application of the requirement for showing a suggestion or motivation to combine references aids in avoiding an impermissible hindsight reconstruction of the claimed invention. *In re Dembiczak*, 175 F.3d 994, 999 (Fed. Cir. 1999).

As indicated within the specification, and hereby in particular within the section “Brief Summary of the Invention” at page 2, lines 7-12 of paragraph [012] of the published application US2004/0076645A1 it states:

[T]he present invention provides a prophylactic and therapeutic mean for the treatment of obesity and related diseases, which is based on an ordered and repetitive ghrelin or ghrelin-derived peptide core particle array and in particular on a VLP-ghrelin/ghrelin peptide-conjugate and -array, respectively.

Sebbel neither discloses nor suggests, or motivates the skilled person in the art to use, ghrelin or ghrelin peptides, wherein said ghrelin peptide comprises an amino acid sequence of SEQ ID NO:119, as antigens or antigenic determinants to form an ordered and repetitive antigen array as required by present independent claim 1; nor does Sebbel disclose, suggest or motivate the skilled person in the art to use ghrelin or ghrelin peptides as antigens or antigenic determinants to form an ordered and repetitive antigen array with virus-like particles of an RNA-bacteriophage by way of non-peptide bond as required by present independent claim 63. Furthermore, Sebbel does not disclose or suggest or motivate the skilled person in the art to use ordered and repetitive antigen arrays comprising ghrelin or

ghrelin peptides associated with core particles as prophylactic or therapeutic means for the treatment of obesity.

Kojima reports the purification and identification of ghrelin as an endogenous ligand specific for growth-hormone secretagogues receptor (GHS-R) (abstract of Kojima). Specifically, Kojima describes the purification procedure, the determination of amino acid sequence of rat and human ghrelin, the characterization of the O-n-octanoylation of serine at position 3, the biochemical property of ghrelin as well its expression pattern in various tissues.

Thus like Sebbel, Kojima neither discloses nor suggests, or motivates the skilled person in the art to use, ghrelin or ghrelin peptides, wherein said ghrelin peptide comprises an amino acid sequence of SEQ ID NO:119, as antigens or antigenic determinants to form an ordered and repetitive antigen array as required by present independent claim 1; nor does Kojima discloses nor suggests or motivates the skilled person in the art to use ghrelin or ghrelin peptides as antigens or antigenic determinants to form an ordered and repetitive antigen array with virus-like particles of an RNA-bacteriophage by way of non-peptide bond as required by present independent claim 63. Moreover, the fact that a claimed species or subgenus is encompassed by a prior art genus is not sufficient by itself to establish a *prima facie* case of obviousness. *In re Baird*, 16 F.3d 380, 382, 29 USPQ2d 1550, 1552 (Fed. Cir. 1994) ("The fact that a claimed compound may be encompassed by a disclosed generic formula does not by itself render that compound obvious."). See MPEP § 2144.08. Furthermore, Kojima does not disclose or suggest or motivate the skilled person in the art to use ordered and repetitive antigen arrays comprising ghrelin or ghrelin peptides associated with core particles as prophylactic or therapeutic means for the treatment of obesity.

There is no reason, suggestion, or motivation in Sebbel or in Kojima that would lead one of ordinary skill in the art to combine the references. Therefore, the Examiner has not met the burden of establishing a *prima facie* case of obviousness based on Sebbel in view of Kojima.

For at least these reasons, the presently claimed invention is not rendered obvious by Sebbel or Kojima, alone or combination. Applicants therefore respectfully request that the Examiner reconsider and withdraw the present rejection of pending claims 1-3, 15, 19, 21-31, 32-34, 55, 63 and 76-85 under 35 U.S.C. § 103.

***(b) Claims 4, 6-8, 11-14, 31, 66, 68-70, 72, 73, 75, and 85 are not rendered obvious under 35 U.S.C. 103(a) as being unpatentable by Sebbel et al. in view of Kojima et al and further in view of Vasiljeva et al. and Maita et al.***

The Examiner has rejected claims 4, 6-8, 11-14, 31, 66, 68-70, 72, 73, 75, and 85 as being obvious over Sebbel in view of Kojima and further in view of Vasiljeva et al. (FEBS Letters, 1998, herein "Vasiljeva") and Maita et al. (Gen Pept Accession VCBPQB, 1971, herein "Maita"). Applicants respectfully disagree. As an initial matter claim 66 has been cancelled, rendering moot the rejection as it may have been applied to those claims. Applicants respectfully traverse the rejection as it may have been applied to the presently pending claims.

Vasiljeva indicates the use of C-terminal UGA extension of the short from of Q $\beta$  coat, so-called A1 extension, as a target for presentation of foreign peptides on the outer surface of mosaic Q $\beta$  particles. However, only the 5 amino acid short preS1 epitope 31-DPAFR-35 of the hepatitis B surface antigen has been disclosed in Vasiljeva (see abstract of Vasiljeva). The short foreign peptide is expressed as a fusion protein with A1. There is nothing in the



reference that discloses or suggests attaching such a 5 amino acid short peptide to the A1 extension or the Q $\beta$  coat protein using a non-peptide bond. Finally, there is nothing in the reference that discloses or suggests attaching ghrelin or ghrelin peptides as antigens or antigenic determinants to form an ordered and repetitive antigen array.

Maita discloses only the amino acid sequence of the coat protein of bacteriophage Q $\beta$ .

For reasons elaborated above, which are entirely incorporated herein by reference, Sebbel and Kojima would not have rendered the claims obvious under 35 U.S.C. § 103. The defects in these references cannot be remedied by Vasiljeva and Maita alone or combination, at least because the Examiner has not demonstrated a motivation to combine Vasiljeva and Maita alone or combination with the other two references with reasonable expectations of success. Moreover, the fact that a claimed species or subgenus may be encompassed by a known genus is not sufficient by itself to establish a *prima facie* case of obviousness. *See In re Baird*, 16 F.3d 380, 382, 29 USPQ2d 1550, 1552 (Fed. Cir. 1994); *see also* MPEP § 2144.08.

For at least these reasons, Applicants respectfully assert that claims 4, 6-8, 11-14, 31, 69-70, 72, 73, 75, and 85 are not rendered obvious under 35 U.S.C. § 103 by Sebbel in view of Kojima et al and further in view of Vasiljeva and Maita. Applicants therefore respectfully request that the Examiner reconsider and withdraw the present rejection of the pending claims.

### ***Conclusion***

All of the stated grounds of rejection have been properly traversed, accommodated or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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